

CLAIMS

1. Antagonists of CXCR3-binding CXC chemokines consisting of mutants of CXCL11, CXCL10, or CXCL9 in which at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 46, 62, 66, and 70.
2. The antagonists of claim 1 wherein CXCR3-binding CXC chemokine is human CXCL11 and at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is additionally substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine: 49, 52, 57, 59, 67, or 71.
3. The antagonists of claim 2 wherein one of the following combinations of basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutamic Acid, Glutamine, Aspartic Acid, or Asparagine:
 - a) 46, together with 49 and/or 52;
 - b) 62, together with 57 and/or 59;
 - c) 66 and 70, together with 67 and/or 71; or
 - d) 62 and 66, together with one or more of the following: 57, 59, 67, 70, or 71.
4. The antagonists of claim 2 or 3 wherein at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is additionally

substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutammic Acid, Glutamine, Aspartic Acid, or Asparagine: 5, 6, 8, 17, 20, 26 or 38.

5. The antagonists of claim 1 wherein CXCR3-binding CXC chemokine is human CXCL10 and at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is additionally substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutammic Acid, Glutamine, Aspartic Acid, or Asparagine: 47, 48, 51, 52, 59, 74, or 75.
6. The antagonists of claim 5 wherein one of the following combinations of basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutammic Acid, Glutamine, Aspartic Acid, or Asparagine:
 - a) 46 and 52, together with 47, 48, or 51;
 - b) 59 and 62;
 - c) 66 and 70, together with 74 and/or 75; or
 - d) 62 and 66, together with 59 and/or 70.
7. The antagonists of claim 5 or 6 wherein at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is additionally substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutammic Acid, Glutamine, Aspartic Acid, or Asparagine: 5, 8, 22, 26, or 38.
8. The antagonists of claim 1 wherein CXCR3-binding CXC chemokines is human CXCL9 and basic residue 67, numbered on the sequence of human mature

CXCL11, is additionally substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutammic Acid, Glutamine, Aspartic Acid, or Asparagine.

9. The antagonists of claim 8 wherein one of the following combinations of basic residues, numbered on the sequence of human mature CXCL11, is substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutammic Acid, Glutamine, Aspartic Acid, or Asparagine:
 - a) 62, together with 66 and/or 67;
 - b) 66 and 67; or
 - c) 66 and 70, together with one or more of the following: 67, 74, or 75.
10. The antagonists of claim 8 or 9 wherein at least one of the following basic residues, numbered on the sequence of human mature CXCL11, is additionally substituted to Alanine, Glycine, Serine, Threonine, Proline, Glutammic Acid, Glutamine, Aspartic Acid, or Asparagine: 5, 6, 8, 25, 28, or 38.
11. The antagonists of claims 1 to 10 wherein the basic residues are substituted with Alanine or Glycine.
12. The antagonists of claim 11 having the sequence of CXCL11-2B3 (SEQ ID NO: 3), CXCL11-3B3 (SEQ ID NO: 4), or CXCL11-4B4 (SEQ ID NO: 5).
13. The antagonists of claims 1 to 12 wherein one or more amino acids that have been added, deleted, or substituted belong to the first nine amino acids in the amino-terminal domain of the human mature CXCR3-binding CXC chemokine.

14. The antagonists of claims 1 to 13 wherein one or more amino acids have been mutated to decrease the aggregation properties of said antagonist.
15. Antagonists of CXCR3-binding CXC chemokines comprising the antagonists of claims 1 to 14, and an amino acid sequence belonging to a protein sequence other than the corresponding CXCR3-binding CXC chemokine.
16. The antagonists of claim 15, comprising an amino acid sequence belonging to one or more of these protein sequences: extracellular domains of membrane-bound protein, immunoglobulin constant region, multimerization domains, extracellular proteins, signal peptide-containing proteins, export signal-containing proteins.
17. Antagonists of CXCR3-binding CXC chemokines comprising peptide mimetics designed on the sequence and/or the structure of the antagonists of claims 1 to 14.
18. Active fractions, precursors, salts, or derivatives of the antagonists of CXCR3-binding CXC chemokines of claims 1 to 17.
19. The antagonists of claims 1 to 18, wherein said antagonist is in the form of active conjugate or complex with a molecule chosen amongst radioactive labels, biotin, fluorescent labels, cytotoxic agents, or drug delivery agents.

20. DNA molecules comprising the DNA sequences coding for the antagonists of claims from 1 to 16, including nucleotide sequences substantially the same.
21. Expression vectors comprising the DNA molecules of claim 20.
22. A host cell transformed with a vector of claim 21.
23. Use of the antagonists of claims from 1 to 19, of the DNA of claims 20 or 21, or of the cells of claim 22, as active ingredients in pharmaceutical compositions for the treatment or prevention of diseases related to excessive leukocyte migration and activation.
24. The use of claim 23 wherein the disease is an inflammatory disease, an autoimmune disease or an infection.
25. The use of claim 24 wherein the disease is multiple sclerosis, rheumatoid arthritis, HIV-1 infection, type I diabetes, or graft rejection.
26. Use of the antagonists of claims from 1 to 19, of the DNA of claims 20 or 21, or of the cells of claim 22, as active ingredients in pharmaceutical compositions for the treatment or prevention of diseases needing an increase of vascularization.
27. The use of claim 26 wherein the disease is an ischemic heart disease.

28. Use of the antagonists of claims from 1 to 19, of the DNA of claims 20 or 21, or of the cells of claim 22, as active ingredients in pharmaceutical compositions for the treatment or prevention of cancer.
29. Process of preparation of antagonists of claims from 1 to 14, comprising culturing the transformed cells of claim 17 and collecting the expressed proteins.
30. Pharmaceutical composition containing an antagonist of CXCR3-binding CXC chemokines of claims from 1 to 19, the DNA of claims 20 or 21, or the cells of claim 22, as active ingredient.
31. Process for the preparation of pharmaceutical compositions for the treatment or prevention of diseases related to excessive leukocyte migration and activation, which comprises combining an antagonist of CXCR3-binding CXC chemokines of claims from 1 to 19, the DNA of claims 20 or 21, or the cells of claim 22, together with a pharmaceutically acceptable carrier.
32. Process for the preparation of pharmaceutical compositions for the treatment or prevention of diseases needing an increase of vascularization, which comprises combining an antagonist of CXCR3-binding CXC chemokines of claims from 1 to 19, the DNA of claims 20 or 21, or the cells of claim 22, together with a pharmaceutically acceptable carrier.
33. Process for the preparation of pharmaceutical compositions for the treatment or prevention of cancer, which comprises combining an antagonist of CXCR3-

binding CXC chemokines of claims from 1 to 19, the DNA of claims 20 or 21, or the cells of claim 22, together with a pharmaceutically acceptable carrier.

34. Method for the treatment or prevention of diseases related to excessive leukocyte migration and activation, comprising the administration of an effective amount of an antagonist of CXCR3-binding CXC chemokines of claims from 1 to 19, of the DNA of claims 20 or 21, or of the cells of claim 22.
35. Method for the treatment or prevention of diseases needing an increase of vascularization, comprising the administration of an effective amount of an antagonist of CXCR3-binding CXC chemokines of claims from 1 to 19 of the DNA of claims 20 or 21, or of the cells of claim 22.
36. Method for the treatment or prevention of cancer, comprising the administration of an effective amount of an antagonist of CXCR3-binding CXC chemokines of claims from 1 to 19, of the DNA of claims 20 or 21, or of the cells of claim 22.